Electrocardiographic Abnormalities in Patients With Myotonic Dystrophy

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In examining the incidence and progression of electrocardiographic abnormalities in 45 patients with myotonic dystrophy, 26 (58%) of whom at entry had at least 1 electrocardiographic abnormality, we found conduction abnormalities in 17 (38%). In 21 patients (47%), new abnormalities developed during follow-up (mean, 4.6 years). The overall incidence of electrocardiographic abnormalities increased to 78%, and the incidence of conduction defects increased to 62%. Second-degree or complete atrioventricular block did not develop in any of the patients. Pseudoinfarction patterns were common at entry and during follow-up and were not correlated with evidence of clinical coronary artery disease. There was no correlation between the presence of electrocardiographic abnormalities and apparent disease severity.

(Florek RC, Triffon DW, Mann DE, et al: Electrocardiographic abnormalities in patients with myotonic dystrophy. West J Med 1990 Jul; 153:24-27)

Myotonic muscular dystrophy is a progressive, genetic, multisystem disease characterized by myotonia, a prolonged contraction of voluntary muscle. Other characteristic manifestations include muscle weakness and atrophy, mental impairment, endocrine dysfunction, cataracts, gastrointestinal abnormalities, testicular atrophy, and frontal baldness.[1] Although clinical cardiac involvement is uncommon, electrocardiographic (ECG) abnormalities have been frequently described[2-10]; they most commonly reflect cardiac conduction system involvement. Data on the progression of ECG abnormalities are limited.[9-11] Previous studies present data from either small series[9,11] or retrospective reviews[2-8] that lack follow-up data.

We determined the prevalence of ECG abnormalities in an unselected group of patients with myotonic dystrophy followed in a neurology clinic, and we prospectively examined the progression of ECG abnormalities during follow-up.

Patients and Methods

In 1979 a registry of all patients with myotonic dystrophy was established at the University of Colorado Health Sciences Center, Denver, Colorado. Entry criteria included myotonia, characteristic muscle involvement (ptosis, nasal speech, orbicularis oculi and oris weakness, neck flexor weakness), or both, and a family history of autosomal-dominant inheritance. At entry and during follow-up, a neurologist took a history and did a physical examination. On follow-up, patients were asked about palpitations, syncope, dyspnea, paroxysmal nocturnal dyspnea, and edema.

For all patients chest x-ray films were taken and standard 12-lead electrocardiograms were recorded at entry and annually during follow-up. Two cardiologists analyzed ECGs independently. First-degree atrioventricular (AV) block, fascicular block, and bundle branch block were diagnosed using standard criteria.[12] Left axis deviation was defined as a frontal plane axis to the left of −30 degrees. Nonspecific interventricular conduction delay was considered present when the QRS complex was longer than 100 milliseconds but shorter than 120 milliseconds. Prolongation of the QRS complex during follow-up was defined as a consistent increase in the QRS duration of at least 20 milliseconds measured in lead V_2. Those Q waves longer than 40 milliseconds and greater than 1 mV in amplitude were considered abnormal. An R/S ratio of greater than 1 in lead V_1 was defined as increased anterior forces.

Electrocardiographic abnormalities were correlated with age and duration of follow-up using an unpaired *t* test and correcting for multiple comparisons.[13] Neuromuscular impairment was assessed by grading for characteristic cranial muscle abnormalities and skeletal muscle strength. Neuromuscular impairment in patients with and without an ECG abnormality was compared with an unpaired *t* test.

Results

Electrocardiographic Abnormalities at Entry

To date, 118 patients from 70 pedigrees have been entered into the registry. The study group consisted of 45 patients (26 men, 19 women; mean age 41 years, range 8 to 63 years) for whom a minimum follow-up of a year was available. Less than one year of follow-up data was available for 73 patients, and they were excluded from analysis. None of the patients received antiarrhythmic therapy during the study period.

Of the 45 patients, 26 (58%) had at least one ECG abnormality on presentation. Left axis deviation was the most frequent abnormality, occurring in 16 patients (36%) (Figure 1). Of these 16 patients, 3 had a QRS axis leftward of −45 degrees and a counterclockwise loop, meeting the criteria for left anterior fascicular block. Left bundle branch block was present in three patients and right bundle branch block in one. Seven patients had a nonspecific interventricular conduction delay. Nine patients (20%) showed first-degree AV block. Abnormal Q waves and increased anterior forces were seen in two and four patients, respectively. A conduction abnormality (first-degree AV block, interventricular conduction delay, fascicular block, or bundle branch block) was present in 17 patients (38%).

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ABBREVIATIONS USED IN TEXT
AV = atrioventricular
ECG = electrocardiographic

Electrocardiographic abnormalities were found in 12 of 25 patients younger than 40 years, with an incidence of 0.64 abnormalities per patient. Of patients older than 40 years, 14 manifested 26 abnormalities, yielding an incidence of 1.3 abnormalities per patient. The incidence of conduction system abnormalities increased significantly with patient age, but even in patients younger than 40 years, 6 of 25 (24%) had a conduction abnormality. Of 20 patients older than 40, 11 (55%) showed conduction abnormalities on their entry ECG. There were no sex differences in the incidence of conduction abnormalities.

Progression of Electrocardiographic Abnormalities

All 45 patients were observed for an average of 55.2 months (range, 12 to 177), or 4.6 years. Of the 45 patients, 36 were followed for at least two years. During the follow-up period, a total of 32 new ECG abnormalities occurred in 21 patients (47%). In eight patients (18%), more than one new abnormality developed. The incidence of any ECG abnormality increased from 58% to 78% during follow-up.

Widening of the QRS complex occurred in 11 patients. New left axis deviation developed in three patients. Abnormal Q waves appeared in three, and the number of patients with increased anterior forces more than doubled, from four to nine. New conduction abnormalities developed in 11 patients. In patients with first-degree AV block at entry, the PR interval was not significantly prolonged during follow-up (PR interval at entry was 0.21 ± 0.02 seconds, mean ± standard error of the mean; PR interval on last follow-up was 0.23 ± 0.03 seconds; *P* not significant), although new first-degree AV block was noted in six patients. In one patient, who had left axis deviation at entry, left anterior hemiblock developed during follow-up. Complete bundle branch block developed in four other patients. The occurrence of nonspecific interventricular conduction delay increased from 16% to 36%. The incidence of bifascicular block increased from 7% to 13% during follow-up. Second-degree or complete heart block did not develop in any patient during the follow-up period.

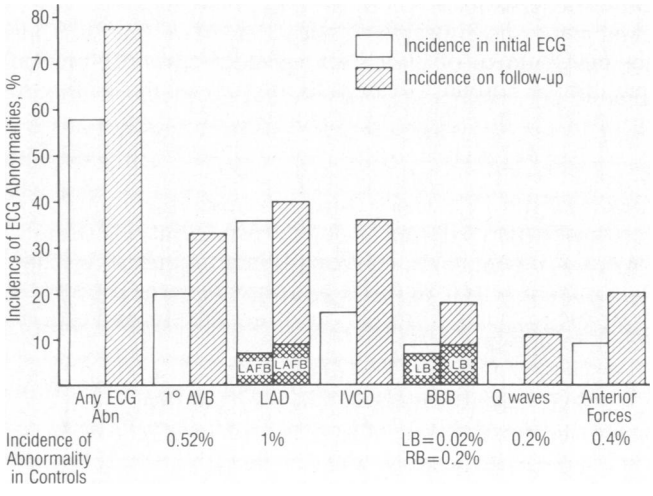

Figure 1.—The chart shows the incidence of electrocardiographic abnormalities at entry and during follow-up in 45 patients with myotonic dystrophy. Shown below the abscissa is the incidence of the electrocardiographic abnormality in 67,375 controls (from Averill and Lamb[14]). Abn=abnormality, 1° AVB=first-degree atrioventricular block, BBB=bundle branch block, ECG=electrocardiogram, IVCD=nonspecific interventricular conduction delay, LAD=left axis deviation, LAFB=left anterior fascicular block, LB=left bundle branch block, Q waves=abnormal Q waves, RB=right bundle branch block

None of the patients had a pacemaker at entry, but five underwent permanent pacemaker placement during the follow-up period. Symptomatic sinus bradycardia (syncope) had developed in one patient, two had asymptomatic sinus bradycardia, one had left anterior fascicular block, and one had first-degree AV block and left bundle branch block. No deaths occurred in the patients not having a pacemaker during the follow-up period. Of those receiving permanent pacemakers, one patient with asymptomatic sinus bradycardia and a family history of sudden death in two affected siblings died suddenly at home. Monitor strips from the emergency department showed pacer spikes at the programmed rate without ventricular capture. The family declined an autopsy. The other four patients who had undergone implantation of a permanent pacemaker remained asymptomatic during follow-up.

Correlation to Disease Severity

Ventricular function was not formally assessed. Only three patients, however, described symptoms of dyspnea, one had edema, and none reported paroxysmal nocturnal dyspnea. On physical examination, none of the 45 patients had signs of right or left ventricular failure. Serial chest x-ray films of 19 patients were available for review and showed normal cardiac silhouette in all but 1 patient, whose cardiac function was normal by radionuclide angiography. Thus none of the patients had evidence of ventricular dysfunction.

No correlation was seen between the presence of ECG abnormalities on entry and the severity of neuromuscular disease as reflected by cranial muscle involvement or muscle impairment. Similarly, there was no relation between the progression of ECG abnormalities and disease severity.

Of the 45 patients, 13 (29%) had experienced palpitations, syncope, or paroxysmal dyspnea on at least one occasion, but the incidence of these symptoms was not significantly different between those with or without ECG abnormalities at entry and those with or without new abnormalities during follow-up. Clinical evaluation, including telemetry and 24-hour Holter examination, failed to show arrhythmias corresponding to these symptoms in any patient. Ambulatory ECG monitoring was done in 12 patients: 4 were normal (except for conduction abnormalities or sinus bradycardia); 3 had asymptomatic, intermittent atrial fibrillation or paroxysmal supraventricular tachycardia (with moderate ventricular response); and 7 (including 2 with supraventricular arrhythmias) had rare to frequent asymptomatic premature ventricular beats. No ventricular tachycardia or ventricular couplets were observed.

Discussion

The prevalence and progression of electrocardiographic abnormalities as reported in this study represent observations in patients with myotonic dystrophy from a neurology clinic cohort unselected for cardiovascular symptoms or abnormalities. Nevertheless, the incidence of ECG abnormalities is higher in patients with myotonic dystrophy than in an otherwise normal control population.[14] Electrocardiographic abnormalities were present in 26 of the patients (58%) on entry in this study. This figure is similar to the 45% to 86% reported in other studies (Table 1).[2-5,7,10] Conduction disturbances—first-degree AV block, interventricular conduction delay, fascicular block, or bundle branch

TABLE 1.—*Incidence of Electrocardiographic Abnormalities in Patients With Myotonic Dystrophy*

Reference Source	Patients, No.	ECG Abnormality, %	Left-Axis Deviation, %	1°AV Block, %	LBBB, %	RBBB, %	Bifascicular Block, %	Complete Heart Block, %
DeWind and Jones, 1950[2]	98	62	..	..	..	..	..	3
Fisch, 1951[3]	85	68	..	48	..	..	..	0
Payne and Greenfield, 1963[4]	47	45	23	11	4*	4*	..	0
Church, 1967[5]	300	86	19	38	11*	11*	..	0.4
Fearrington et al, 1964[7]	17	70	30	30	..	..	..	0
Moorman et al, 1985[10]	46	72	9	33	0	2	..	0
Present study								
At entry	45	58	36	20	7	2	7	0
During follow-up	45	78	40	33	9	9	13	0

AV=atrioventricular, ECG=electrocardiogram, LBBB=left bundle branch block, RBBB=right bundle branch block

*The patients in these two studies had both right and left bundle branch block.

block—were the most common finding (17 patients, or 38%) and increased with time.

Previous studies on the progression of ECG abnormalities in patients with myotonic dystrophy suggest a slow progression of conduction system disease. Moorman and co-workers[10] retrospectively reviewed previous (4 months to 13 years) ECGs in 30 patients and found a prolongation of the QRS duration in 2 persons and the development of 2:1 AV block in 1. They found no evidence of a progression of ECG abnormalities in the other 27 patients. Prystowsky and associates examined nine patients with serial electrophysiologic studies, a mean of 35 months apart.[11] At the second study, more patients had a prolonged infranodal conduction time. The course of the progression was unpredictable, however, and clinically significant block did not develop in any patient. Örndahl and colleagues reported a slow increase in both PR interval and QRS duration over 1 to 26 years in 23 patients.[15]

This is the first prospective analysis of the progression of ECG abnormalities in a large population of patients with myotonic dystrophy. Electrocardiographic changes developed at a rate of about one new abnormality for every six patients with myotonic dystrophy per year. New conduction disturbances occurred in 11 patients (24%), and the overall prevalence of first-degree AV block, interventricular conduction delay, and fascicular or bundle branch block increased from 38% to 62%. The incidence of bifascicular block nearly doubled, but none of the patients showed complete heart block on entry or during the follow-up period.

The low incidence of high-grade block noted is consistent with that of other prospective studies.[9-11] Higher frequencies of complete heart block have been reported in literature reviews such as that of DeWind and Jones, who reported a 3% incidence.[2] Retrospective literature reviews, however, probably overestimate the actual incidence of the infrequent phenomenon because it is more often reported. Anecdotal reports of complete heart block in patients with myotonic dystrophy[16-20] are difficult to interpret. In at least two of these cases, AV block developed before other features of myotonic dystrophy in patients who were in their 50s.[16,17] The causal relationship of myotonic dystrophy in these cases may be questioned because idiopathic conduction system disease can also be observed in this age group.[21]

Sudden death is reported in 0% to 4% of patients with myotonic dystrophy[10] and is frequently ascribed to the development of complete heart block. In light of the apparently rare occurrence of high-grade AV block, we think other possible causes of sudden death may be more important. This view is supported by several observations. First, we and others have noted that sudden death may occur despite the presence of a pacemaker.[9,22,23] In the case we report, there was no evidence of pacemaker malfunction. Second, other possibly fatal abnormalities can occur in patients with myotonic dystrophy, including sleep apnea and pulmonary hypertension,[24] mitral valve prolapse,[25] left ventricular failure,[5,22,23] and ventricular arrhythmias. In several cases of monitored sudden death or syncope, including those reviewed by Moorman and co-workers,[10] ventricular arrhythmias have been documented as the cause of death. In several case reports, potentially lethal ventricular arrhythmias have been recorded in patients with myotonic dystrophy by ambulatory monitoring[5,17,20,22,23] or by invasive electrophysiologic evaluation.[26] Nevertheless, no prospective study has defined the incidence of either spontaneous or inducible ventricular arrhythmias in these patients. The role of ventricular arrhythmias in patients with myotonic dystrophy remains speculative, but we think it has probably been underestimated.

Electrocardiographic patterns suggestive of coronary artery disease (pathologic Q waves or increased anterior forces) were present in five of our patients (11%), although the mean age of this subgroup was 43 years and no ischemic symptoms were present. New pathologic Q waves and increased anterior forces developed in eight patients (18%), and their overall incidence increased from 11% to 27%. Only two patients had clinical signs of coronary artery disease, and none appeared to have congestive failure. Thus the development of ECG features suggestive of infarction and clinical coronary artery disease may be misleading in this group[7] and should be interpreted with care.

There appears to be no correlation between the degree of disease severity and the presence or progression of ECG abnormalities in patients with myotonic dystrophy. This conclusion, derived from an objective observation of neuromuscular involvement, confirms similar impressions made on the basis of retrospective literature reviews.[5,8,9] Apparently the pathologic process can affect skeletal and cardiac tissue to different degrees.

Electrocardiographic abnormalities in patients with myotonic dystrophy frequently progress even during a relatively short follow-up. Most abnormalities are, however, clinically insignificant conduction disturbances, the development of pseudoinfarction patterns without clinically apparent coronary artery disease, and widening of the QRS complex. Nevertheless, these results should be interpreted with caution because no extensive evaluation of ventricular function was done in our patient population, these patients were relatively young (though typical for a similarly affected patient population), and the follow-up period was short for this chronic neuromuscular disease.

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